SUMMARY OF TESTIMONY OF

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CHAIRMAN AND CEO, BARR PHARMACEUTICALS, INC.

"FDA FOREIGN DRUG INSPECTION PROGRAM: A SYSTEM AT RISK"

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

NOVEMBER 1, 2007

- Changes to the FDA Foreign Inspection process must recognize that the U.S. generic pharmaceutical review and approval system is very sound and is not broken. Modifications to Foreign Inspections must be undertaken in a manner that ensures a fair and level playing field.
- We are committed to working with Congress and FDA to implement needed and appropriate changes that will result in a system that treats all manufacturers, and all parts of the pharmaceutical supply chain, equally with respect to the integrity of all medicines.
- Recommendations to the Subcommittee:
  - The consideration of new funding sources, including discussion of the value of potential user fees applied broadly and fairly. Such a system, if carefully crafted and implemented, could ensure that FDA has the requisite resources to conduct cGMP and pre-approval foreign inspections of foreign facilities to the same extent and same rate and to the same standard as that of domestic companies.
  - The consideration of a DMF Type II: API user fee or API establishment fee to ensure that FDA has the necessary resources to conduct inspections of API suppliers. The user fee could be a source of funding for increasing the foreign inspection safety net, with companies forfeiting a portion of their user fee if a DMF application was found to be materially deficient. Additionally, the allocation of a payment as part of a separate user fee structure would ensure that FDA had sufficient funds to inspect all entities in the business of APIs as well as finished prescription drug products, and would further motivate API manufacturers to ensure the quality of API and other raw materials targeted for the United States.
  - FDA should continue to implement a Risk Based Inspection System for better allocation of currently scarce resources, based on both the portfolio of products produced and the record of compliance. Companies with strong records of compliance and positive inspections would be permitted to proceed to market with their products in the U.S. based upon this track record, without delays resulting from waiting for FDA pre-approval or surveillance inspections on every product. At the same time, this system would ensure that questionable or problematic facilities receive a comprehensive review and evaluation.

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Good morning Chairman Stupak, Ranking Member Whitfield and Members of the House Subcommittee on Oversight and Investigations. Thank you for inviting me to discuss FDA's Foreign Drug Inspection Program – a program that is critical to ensuring the integrity of the American drug supply.

My name is Bruce Downey and I am Chairman and Chief Executive Officer of Barr Pharmaceuticals, a leading global manufacturer of generic and brand name prescription drugs, as well as over-the-counter medicines. Barr currently operates in more than 30 countries, with manufacturing and packaging operations of finished dosage forms in multiple sites in the United States, and manufacturing of Active Pharmaceutical Ingredients (APIs) and finished dosage form products in Croatia, Poland and the Czech Republic.

I am also Chairman of the Generic Pharmaceutical Association, which represents domestic and multinational companies that manufacture ninety (90) percent of the FDA-approved generic pharmaceuticals dispensed in the United States, as well as active ingredient suppliers for this market.

The U.S. generic pharmaceutical industry is committed to ensuring that the medicines we provide to consumers are of the highest quality and safe and effective for their intended use. In the United States, patients have rightfully come to expect that when they go to their local pharmacy counter they will receive the highest quality, FDA-approved prescription drug products in the world.

Millions of Americans rely on FDA-approved medicines everyday to improve their quality of life, treat illnesses and extend life. High-quality, affordable FDA- approved generic drugs have opened the doors for access to needed medicines for countless of our citizens, especially seniors, many of whom could not previously afford their medications. The record is clear that FDA-approved generic drugs consistently offer the same quality, safety and therapeutic effectiveness as their brand counterparts and, in the process, save tens of billions of dollars each year for insurers, taxpayers, Medicaid and Medicare, and cash-paying consumers.

I believe that I can speak on behalf of the generic pharmaceutical industry when I assure this committee that our industry invests hundreds of millions of dollars annually into state-of-the-art research and development and manufacturing facilities; maintaining complex operational infrastructures to ensure product

quality and efficacy; retaining highly skilled and dedicated employees; and developing and implementing extensive quality control systems. Last year, 63% of the 3.6 billion new and renewal prescriptions dispensed in the U.S. were filled with generics. That's approximately 2.3 billion generic prescriptions that were used safely and effectively by patients and consumers across the country.

We manufacture our products to exacting standards -- lot-to-lot -- that have been reviewed and approved by FDA through the drug application process. Over the last decade, our highly regulated industry has demonstrated its commitment to adhering to the highest quality standards for prescription drugs in the world – and our compliance track record over the last five years is second to none.

As Chairman of a multinational, global company, I'm here today to applaud the bipartisan efforts of this Committee in taking an affirmative oversight role with respect to the integrity of this nation's prescription drug supply and to reiterate our long standing commitment to doing our part.

In my testimony, I want to make several key points.

First, changes to the FDA Foreign Inspection process must recognize that the U.S. generic pharmaceutical review and approval system is very sound and is not broken, and that any modifications to Foreign Inspections must be undertaken in a manner that ensures a fair and level playing field. As a trusted pharmaceutical company, Barr, as well as all of the members of the generic pharmaceutical industry, are committed to ensuring that only the highest quality products, approved by the FDA, reach American consumers. We must meet very exacting product manufacturing and testing standards to ensure this and we hold our suppliers and active pharmaceutical ingredient suppliers to very exacting standards. We are perhaps the most highly regulated aspect of the current system, from the FDA requirements related to product development, application filing, final approval and post-marketing surveillance.

Second, while we applaud the FDA's ongoing efforts to remove unapproved products from the market, additional measures must be taken to prevent all counterfeit and unapproved products from being marketed to U.S. consumers and placing them at risk. This situation is untenable and must be addressed. We have several proposals to offer to assist this committee, and the FDA, in closing these gaps.

Third, we must meet very exacting product manufacturing and testing standards to ensure this. We are committed to working with this committee, as well as all members of Congress and the FDA, to implement needed and appropriate changes that will result in a system that treats all manufacturers, and all parts of the pharmaceutical supply chain, equally with respect to the integrity of all medicines.

Changes to the FDA Foreign Inspection process must recognize that the domestic system we adhere to is the best in the world and that any modifications must ensure a fair and level playing field with the goal of ensuring access, safety and efficacy.

We support the goal to give FDA adequate resources to test products, inspect facilities and perform the requisite oversight of foreign finished dosage forms and API manufacturers. I want to state for the record, however obvious, that quality cannot be tested into the product at the border. Foreign inspection must be as inclusive and robust as the strictly controlled processes that FDA requires of domestic manufacturers, including the assurance that products are made in facilities that have the proper core competencies, laboratories, and operational

manufacturing and quality systems to ensure total control over every facet of the development and manufacturing of every product we market.

BACKGROUND

Manufacturers of FDA-approved drug products operate in a highly regulated environment. FDA promulgates strict rules governing the development, manufacture, approval, packaging, marketing and post-marketing surveillance of prescription drugs. And to ensure the highest purity and quality, FDA has in place rigorous inspection standards for facilities that manufacture and supply prescription drugs.

While these stringent regulations apply equally to all brand, generic and biological prescription drugs approved by the FDA, there are drugs sold today in the U.S. without FDA's approval. These unapproved and unregulated products include, but are not limited to, counterfeit drugs and certain prescription drugs sold over the internet.

As this Committee knows, federal law requires that generic drugs have the same active ingredients, same dosage form, same standards for purity and quality,

same standards for manufacturing, and same amount of medicine absorbed into the body over the same time as the equivalent brand product.

In other words, to receive FDA approval, the FDA-approved generic must perform in the patient in the same manner as the innovator drug. This means the same amount of active ingredient must reach the bloodstream in the same time as the brand, and must remain in the bloodstream for the same length of time as the brand. While generics may occasionally be a slightly different size, shape or color than their brand counterparts to avoid trade-dress issues, these cosmetic differences have no impact on the safety or effectiveness of a generic prescription drug.

As the CEO of a company that manufactures both brand and generic prescription drugs, I can attest that the approval process for generics is equally as rigorous as it is for brand drugs. I can say further that all prescription drug manufacturers, both brand and generic, expend considerable resources for self-policing their operations through the auditing of vendors, testing of incoming materials, and completing quality programs in order to comply with FDA regulations.

The penalties for non-compliance are significant. Here in the U.S., CEOs and other senior management can be held criminally liable for any misconduct related to manufacturing prescription drugs. In addition, non-compliance can result in business interruptions that can cost tens of millions of dollars in earnings and can severely damage reputations.

INSPECTIONS

The Federal Food, Drug and Cosmetic Act (FDCA) requires FDA to conduct Current Good Manufacturing Practice (cGMP) inspections of all domestic prescription drug manufacturing sites every two (2) years. CGMP inspections provide the assurance that each product we market has the same quality, strength and purity as the product approved by FDA and that it is manufactured and tested in accordance to exact FDA-approved methods and standards.

In addition, in our highly regulated sector, there are also pre-approval product inspections for both brand and generic products – products that are subject to abbreviated or new drug applications. And there are the unannounced, periodic inspections to ensure companies continually remain cGMP compliant, and these

inspections can take anywhere from several weeks to months. Inspections are a vital component of the regulations that govern the brand and generic industries.

Unfortunately, FDA faces the serious challenge of having severely limited resources to undertake the much needed inspections of foreign facilities that manufacture finished dose and active pharmaceutical ingredients supplied to the U.S. market. Recent data presented by the FDA shows that while the number of foreign sites exporting pharmaceutical products to the U.S. has increased dramatically over the past decade, the number of FDA inspections of these sites has declined.[1]

For instance, in 2000 there were 1,436 cGMP inspections of domestic drug manufacturers and 248 foreign inspections. By 2004, the number of domestic inspections had risen to 1,825, but the number of foreign inspections had dropped to 184. [2] These data are more striking when considering that, in 2004, there were 2,700 foreign drug manufacturers registered with the FDA, compared to 3,300 registered domestic manufacturers.[3]

[1] FDA Perspective: High Priority Topics & Future Directions, Deborah Autor, Director, CDER Office of Compliance, October 10, 2007.
[2] CDER Reports to the Nation, 2004.
[3] Citizen Petition, Synthetic Organic Chemical Manufacturers Association, January 24, 2006, pg. 2.

In direct contrast to domestic inspections, foreign inspections are generally announced to the company many weeks, if not months, prior to that inspection, and only last for three (3) to five (5) days, with little to no follow-up inspections. By comparison, domestic inspections are unannounced, and frequently last longer than 5 days -- many routine domestic inspections can last for weeks.

A significant cause for the inadequate foreign inspection rate is that the U.S. has no statutory requirement that overseas plants be inspected. Further, FDA has no jurisdiction over foreign facilities. The FDA just does not have the manpower or financial resources needed to conduct even a reasonable number of foreign inspections. Indeed, FDA Deputy Commissioner Randall Lutter, in September testimony to the Committee on Energy and Commerce, remarked that some foreign companies that export medicines to the U.S. have not been inspected by the FDA in as many as 10 years. Furthermore, FDA has no inspectors permanently dispatched to India and China, despite these nations' rapidly expanding pharmaceutical industries. And lastly, when foreign facilities do get inspected, the outstanding question is whether FDA applies a lesser cGMP standard to those facilities than to domestics.[4]

[4] See 1993 FDA internal memorandum and 1998 GAO report.

This imbalance between domestic and foreign inspections creates a potential competitive advantage for manufacturers operating overseas where inspections are less frequent and liability less risky. Therefore, leveling the playing field in terms of domestic and foreign inspections should be one of the objectives as we move forward with this effort.

FDA APPROVAL OF RAW MATERIALS USED IN GENERIC APPLICATIONS

A critical component of generic pharmaceutical development, approval and marketing in the United States is the sourcing of the active pharmaceutical ingredient in the generic product. Here, ensuring that the source of the API can provide an approvable, reliable source of active ingredient is critical to success for the generic pharmaceutical manufacturer.

GMP compliance of the API manufacturer is critical. If a GMP deficiency is found at the API manufacturer, the approval of a generic product is delayed. Frequently, a generic manufacturer in the U.S. will invest in the processes necessary to ensure GMP compliance in its API suppliers. However, the API supplier must be GMP compliant before production can begin on the active

pharmaceutical ingredient that is to be included in the generic company's application for approval with the FDA.

Once GMP compliance is assured, the generic pharmaceutical company analytical research scientists analyze incoming materials to ensure that current and future supplies will consistently comply with quality requirements, including stability and process requirements. Sophisticated analytical methods are developed and implemented to ensure purity and quality. All of these sophisticated, scientific requirements become part of the Drug Master File, referenced in the generic application. This ensures the quality and purity of the active pharmaceutical ingredient in FDA-approved generic drugs.

U.S. GENERIC PHARMACEUTICAL COMPANIES SELF-POLICE THEIR PROCESSES AND PRODUCTS

In addition to FDA and numerous other regulatory requirements, generic manufacturers invest heavily in self-policing the sources of material and processes used. To assure the purity of the active and other ingredients, generic pharmaceutical manufacturers extensively conduct due diligence throughout the supply chain. The industry audits vendors to assure the quality and purity of all

active ingredients and other raw materials used in its manufacturing of prescription pharmaceutical products, including rigorous testing of incoming materials and assuring purity with Certificates of Analyses.

I strongly urge Congress to recognize the need to increase foreign inspection resources without cannibalizing the inspection of the generic pharmaceutical API supply chain.

While the generic prescription pharmaceutical industry takes extensive steps to ensure that our source materials and finished drug products are of the highest quality and are safe and effective for their intended use, FDA can and should supplement our actions with routine compliance inspections to: (1) validate our determinations of suppliers' compliance; (2) shore up potential missed system deficiencies; (3) facilitate pre-approval product inspections in a timely manner.

RECOMMENDATIONS

We recognize the risk of foreign-made, inadequately inspected, active chemical ingredients and finish dose drugs being introduced into the American supply chain. We support the laudable goal and underlying tenets of Congressman Dingell's Food and Drug Import Safety Act of 2007, H.R.3610. To this end, we

strongly support providing substantial funding to FDA's foreign inspection program, to ensure that FDA's quality standard is the world's gold standard. But we respectfully remind this subcommittee that any initiatives designed to improve the quality of products purchased by consumers must balance the benefits of the current processes under which America's generic pharmaceutical industry has built a bond of trust and service to consumers.

Modifications that would disproportionately place the burden on the generic pharmaceutical sector, such as the import line item fee or any other measure that would negatively impact the ability of companies to source high quality raw materials, could have negative consequences to our industry's ability to get new, affordable, FDA-approved generic products to market on a timely basis.

As I previously stated, while we believe that our FDA-approved prescription products adhere to the highest quality standards in the world, there is room for significant improvement in FDA's foreign inspection program. Our recommendations for improvements are as follows:

1. The consideration of new funding sources, including discussion of the value of potential user fees applied broadly and fairly. Such a system, if carefully

crafted and implemented, could ensure that FDA has the requisite resources to conduct cGMP and pre-approval foreign inspections of foreign facilities to the same extent and same rate and to the same standard as that of domestic companies.

2. The consideration of a DMF Type II: API user fee or API establishment fee to ensure that FDA has the necessary resources to conduct inspections of API suppliers. Under this proposal, the user fee could be a source of funding for increasing the foreign inspection safety net, with companies forfeiting a portion of their user fee if a DMF application was found to be materially deficient. Additionally, the allocation of a payment as part of a separate user fee structure would ensure that FDA had sufficient funds to inspect all entities in the business of APIs as well as finished prescription drug products, and would further motivate API manufacturers to ensure the quality of API and other raw materials targeted for the United States.

3. We also would propose that in the interim, FDA continue to implement a Risk Based Inspection System for better allocation of currently scarce resources, based on both the portfolio of products produced and the record of compliance. Under this system, FDA would concentrate efforts on

inspections of companies producing complex products, as well as records of compliance. Companies with strong records of compliance and positive inspections would be permitted to proceed to market with their products in the U.S. based upon this track record, without delays resulting from waiting for FDA pre-approval or surveillance inspections on every product. At the same time, this system would ensure that questionable or problematic facilities receive a comprehensive review and evaluation.

SUMMARY

America's generic pharmaceutical companies have a legal responsibility to ensure that our products are of the highest quality and are safe and effective. If we did not meet the rigorous requirements imposed by the FDA, our products could not receive approval and could not reach consumers.

As a result of FDA regulations, the generic pharmaceutical supply chain is perhaps the most rigorously tested process in product manufacturing in the world. In addition, we also have a fiduciary responsibility to our shareholders and a commitment to the public trust. That is why, in addition to the layers of specifications we meet for FDA approval, we are also committed to comprehensive internal auditing, evaluation, testing and due diligence programs to ensure that all

materials, including the active ingredients, are being procured from cGMP compliant facilities and meet FDA and our standards.

We are also consumers. And we fully recognize the need for increasing FDA inspection of products that are arriving in the United States, and are used by all consumers, that do not have the same hurdles to overcome as generic medicines. As an industry, we are committed to working with Congress to ensure that FDA has adequate resources to conduct foreign inspections that ensure not only the quality of our products, but of foreign-produced products as well.

In making this commitment to Congress, we are cognizant of the fact that balancing these competing demands for resources from FDA foreign inspectors could place the timely availability of U.S. generic pharmaceuticals at risk for delays. Therefore, our recommendations clearly support initiatives that recognize the rigorous nature of the regulations that we must meet, but also the need to formulate solutions that do not unintentionally damage our ability to supply high quality, effective and less costly medicine to consumers in a timely manner.

We seek to ensure that any modifications to the Foreign Inspection Process recognize the efforts expended by the generic pharmaceutical industry, and the

assurance of this committee that any modifications to the system will treat all manufacturers and all parts of the process equally. Failure to infuse adequate resources and implement reform measures will perpetuate a system where there is one standard for domestic FDA-approved prescription drug manufacturers and a lesser standard for foreign manufacturers. Our Foreign Inspection Process is only as strong as its weakest link, and we encourage this committee to focus on those areas where gaps of resources currently permit unapproved and unregulated products, including counterfeit drugs, to reach consumers.

Thank you. I would be happy to address any questions of the Committee members.

Bruce L. Downey
Chairman and Chief Executive Officer
Barr Pharmaceuticals, Inc.

Bruce L. Downey is Chairman of the Board and Chief Executive Officer of Barr Pharmaceuticals, Inc., a global specialty pharmaceutical company that operates in more than 30 countries worldwide and is engaged in the development, manufacture and marketing of generic and proprietary pharmaceuticals, biopharmaceuticals and active pharmaceutical ingredients. A holding company, Barr operates through its principal subsidiaries: Barr Laboratories, Inc., Duramed Pharmaceuticals, Inc. and PLIVA d.d. and its subsidiaries. The Barr Group of companies markets more than 115 generic and 25 proprietary products in the U.S. and more than 1,200 products globally outside of the U.S.

Mr. Downey joined Barr in 1993 as President and Chief Operating Officer and was named Chairman and CEO one year later. For three years prior to joining Barr, Mr. Downey served as the Company's legal counsel.

Prior to joining Barr, Mr. Downey was a partner in the law firm of Bishop, Cook, Purcell and Reynolds. In 1991, when Bishop, Cook merged with the law firm of Winston & Strawn, Mr. Downey became a capital partner in the firm. In 1979, he founded Baller & Downey, which later merged with Bishop, Cook, Purcell & Reynolds. With a law practice in the area of civil litigation, Mr. Downey has represented corporate clients on a broad range of issues before federal and state courts and agencies of the federal government.

Mr. Downey began his legal career in the Honors Program at the United States Department of Justice. He later worked as a Special Litigation Counsel at the United States Department of Energy. While in government service, Mr. Downey received four awards for special achievement.

Mr. Downey graduated with honors from Miami University in 1969 and received his law degree cum laude from Ohio State. He also served on the Board of Editors of the Ohio State University Law Journal and was elected to the Order of the Coif. Mr. Downey is a former director of Warner Chilcott. He currently serves as the Chairman of the Board for the Generic Pharmaceutical Association (GPhA), the trade association for the generic pharmaceutical industry, and as the Chair of the Board of Ambassadors for Johns Hopkins' Project RESTORE that funds research and clinical trials to support the creation of progressive treatments for transverse myelitis and multiple sclerosis.